This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 215

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. CERTIFICATE NUMBER: 93-R-0056
CUSTOMER NUMBER: 1171

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

COPY FOR YOUR INFORMATION

Alza Corporation
1900 Charleston Road (b)(2)High, (b)(7)(F)
Mountain View, CA 94043

(a)
Forde-Falle

Telephone: (b)(6), (6)(7)(C)

"A" by K. Garland 02/14/06 MK

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation, or held for these purposes. Attach additional sheets f necessary)

FACILITY LOCATIONS (Sites) - See Atached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY **(Attach additional sheets if necessary or use APHIS Form 7023A)**

A. Animals Covered By The Animal Welfare Regulations	B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals an for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this repor	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs	Ø	23	23	Ø	46
5. Cats	Ø	Ø	Ø	Ø	Ø
6. Guinea Pigs	85	884	642	2	1528
7. Hamsters	Ø	Ø	Ø	Ø	Ø
8. Rabbits	25	52	79	Ø	131
9. Non-human Primates	Ø	Ø	Ø	Ø	Ø
10. Sheep	Ø	Ø	Ø	Ø	Ø
11. Pigs	4	Ø	Ø	Ø	Ø
12. Other Farm Animals	Ø	Ø	Ø	Ø	Ø
13. Other Animals	Ø	Ø	Ø	Ø	Ø

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and app Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary in brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)

SIGNA	CIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED
(b)(6) (b)(7)(c)		(b)(6) (b)(7)(c)	11/16/05

APHIS F -23 (OCT 88), which is obsolete.
(AUG 91)

NOV 17 2005

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 93-R-0056

2. Number 7 (2=E) of animals used in this study.

3. Species (common name) Hairless Guinea Pig of animals used in the study.

4. Explain the procedure producing pain and/or distress.

Topical application of a transdermal system containing test material.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

This was a safety study performed in 7 animals in accordance with the CFR listed in Section 6.0. One animal had a marked decrease in body weight measured after 1 wk of system application. The animal was euthanized at this time point; end of study. Another animal died unexpectantly; cause of death undetermined.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: Consumer Product Safety Commission, CFR: 16 CFR Part 1500.41, Federal Substances Act, Chapter II, Title 16

COPY FOR YOUR INFORMATION

08 Feb 06

Kathleen M. Garland, VMO
Supervisory Animal Care Specialist
Western Region, Animal Care
2150 Centre Ave., Building B
Mail Stop #3W11
Ft. Collins, CO 80526

Certificate number: 93-R-0056

Dear Dr. Garland,

In response to your letter dated 01 Jan 24 requesting corrected or additional information for our Annual Report (APHIS Form 7023) submitted 11 Nov 05, we submit the following information and clarifications for Column E explanations:

The test referenced in items 5 and 6; 16 CFR Ch11 - 1500.41, is the Consumer Product Safety Commission Method of testing primary irritant substances. The test defines the test system (albino rabbits), application of substance being tested, minimum numbers of animals to be used and approximate quantity of substance to apply. It also describes the periods of observations (24 to 72 hrs) and a scoring system to use to arrive at a primary irritation score. Your letter requests further information concerning:

a. **The use of the guinea pig instead of the rabbit** - The ALZA animal care and use protocol describes the use of this test with hairless guinea pigs as described in the publication: Buehler EV, Kreuzman JJ. Comparable sensitivity of hairless and Hartley strain guinea pigs to a primary irritant and a sensitizer. J Toxicol Cutan Ocul Toxicol 1990; 9(3):163-168. The use of hairless guinea pigs instead of albino rabbits is a refinement since the use of a hairless animal model reduces the irritation due to hair removal through shaving, clipping or use of depilatory agents, which may also interfere with test agent results interpretation. There are no hairless rabbits available as defined laboratory animals. This refined test system has been well established and accepted by past FDA submissions by ALZA.

b. **Extending the test to one week** – the test describes the period of observation to be up to 72 hours but does not specify that the test systems (animals) must be euthanatized at the end of the 72-hour observation period. Animal disposition is not specified at all. The ALZA animal care and use protocol fully describes the test, the length of time the animals will be observed as well as the animals' final disposition. The animals are not required to be euthanatized at the end of each observation period, but at the end of the study as described in the approved animal care and use protocol. The duration of the study mimics the intended clinical study duration.

ALZA CORPORATION 1900 CHARLESTON ROAD P.O. BOX 7210 MOUNTAIN VIEW CA 94039-7210 PHONE 650.564.5000 http://www.alza.com

c. **The use of pain and/or distress relieving drugs and interference with the study outcome or the interpretation of the test** – This test is defined by the Federal Code of Regulations as noted above. No analgesic use is described in the test. The dosing procedure itself is not painful beyond that produced by routine procedures such as injections, but the reaction caused by the test material might cause pain. Therefore, these animals are categorized retrospectively when the response to the test can be observed. In this case, two animals appeared to have possibly experienced some unrelieved pain and/or distress. The one died suddenly before euthanasia could be provided and the other was euthanatized in recognition that its weight loss indicated possible pain and distress, and in keeping with guidelines described in the animal care and use protocol. Therefore, they were retrospectively placed in the Category E column. Intervention compatible with the scope of the Federal safety test and humane animal care and use standards was supplied as possible.

Please let us know if further information is needed or would be helpful. If you have questions,

(b)(6) (b)(7)(c)

Sincerely.

(b)(6) (b)(7)(c)